

Anemia

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Hematology/oncology



Case

HPI

28 yo previously healthy male

- a. Headache, fatigue/ SOB in May
- b. Pancytopenia and massive splenomegaly: hgb ~4, leukopenia, thrombocytopenia
- c. transferred to NWM MICU 5/14



case

- **Past Medical History:**
none
- **Past Surgical History:**
none
- **Allergies:**

NKDA



Case

- **Home Medications:**
none
- **Family History:**
neg
- **Social History:**
+ tob 1/2 ppd x10 yrs
- etoh/drugs



Case

Review of Systems

General: No weight loss, fevers; + worsening fatigue for past 3-4 months

Skin: No rashes, bruises

HEENT: No sore throat, rhinorrhea

Neck: No stiffness

Respiratory: SOB, no cough, sputum, hemoptysis, wheezing

Cardiac: No chest pain, orthopnea, PND

Gastrointestinal: No nausea, vomiting, diarrhea, constipation, hematochezia, melena, BRBPR

Urinary: No hematuria, dysuria, polyuria, incontinence, nocturia

Musculoskeletal: No myalgias, arthralgias

Neurologic: episode of headache, No vision loss, no hearing loss. No numbness, tingling, parasthesia, anesthesia

Hematologic: No bruising, gingival bleeding

Endocrine: No heat/cold intolerance

Psychiatric: No depressed mood



Case

Physical Exam

VSS

Gen: Pale, well-nourished, NAD lying in bed w facial piercings

Skin: pale, mildly jaundice, scattered tattoos

HEENT: PERRL, MMM, no oral lesions noted, slightly
icteric sclerae

Lymphatic: no cervical, supraclavicular LAD, +left sided axillary LAD

Chest : CTAB

Cardiovascular: RRR, no m/r/g

Abdomen: soft, non tender, non-distended, bs+, -hepatomegaly,
+ splenomegaly to pubic rim

Extremities: no pitting edema/clubbing

Neurologic: non focal

Psychiatric: alert and oriented x3



Case

Lab (OSH)

5/13

CBC: 2.2/4.9/78 (DD-) MCV 103

TSH nl

HIV neg



Case

Studies (OSH)

5/13 CT C/A/P

- L axillary LAD, no PTX, pleural effusion, or consolidation
- Marked splenomegaly measuring 24.9cm
- periaortic and celiac region adenopathy

5/13 CT Brain--Neg



Case

PET:

1. There is bilateral axillary lymphadenopathy demonstrated, corresponding to prominent nodes on CT. While non-specific, these findings may be seen with lymphoma. Correlation with biopsy findings is recommended.
2. The remainder of the study demonstrates only subtle additional sites of lymphadenopathy in the iliac regions bilaterally, epigastric region and splenic hilum, as discussed above. Specifically, the focal area of prominent uptake in the region of the gastrohepatic ligament is much less extensive than the soft tissue abnormalities in this region on the CT study. These findings suggest the possibility of a lower grade lesion.
3. There is again noted to be marked splenomegaly with moderate, diffusely increased FDG uptake throughout the spleen. This finding is non-specific in nature, and could reflect lymphomatous involvement or non-specific immune stimulation.



Case

DEEP BREATH!!



Case

Lab 5/14

CBC: **wbc 2.2 Hgb 3 Hct 9, plt 76** ,
MCV 96, DD: -

Reti 17.8, T Bil 2.7, D Bil 0.2, LDH 207, Hapto 17

PT 19.2, INR 1.3, PTT 34.4, FN 469, DD 280

Peripheral smear, BM Bx

Comp- (e T bil), uric acid nl, UA neg w urobilinogen +

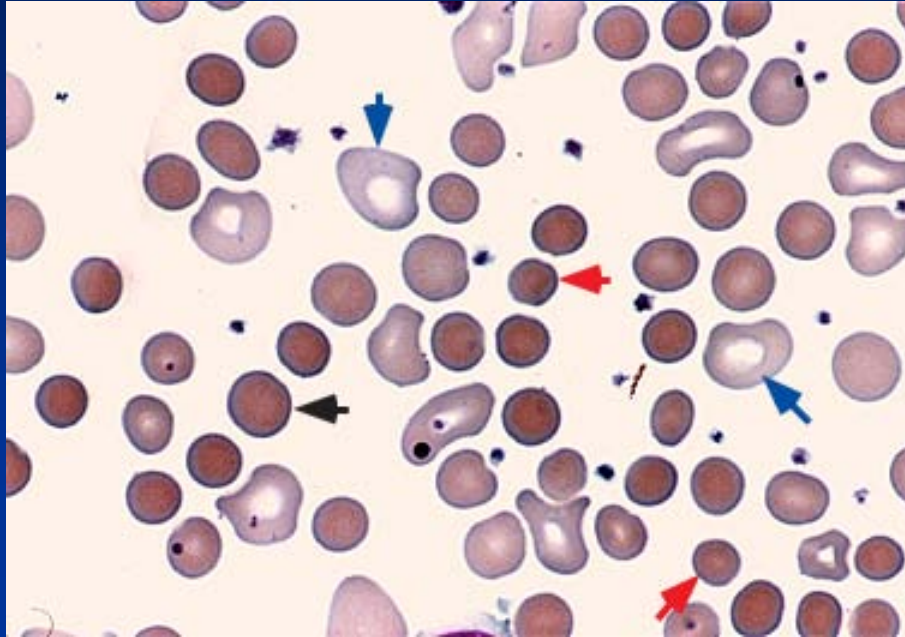


Normal Smear



Normal peripheral blood smear.

Peripheral smear



peripheral blood smear from a similar patient

Case

WARM AUTO-ANTIBODY PRESENT

- *DAT, 2+*
- *DAT, ANTI-IgG COOMBS SERUM: 2+*

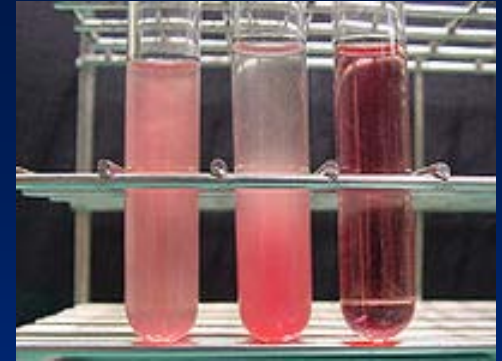


Terminology

- Hemolysis
 - a. hereditary
 - b. acquired
- Autoimmune hemolysis
- Warm-antibody autoimmune hemolysis



Hemolysis



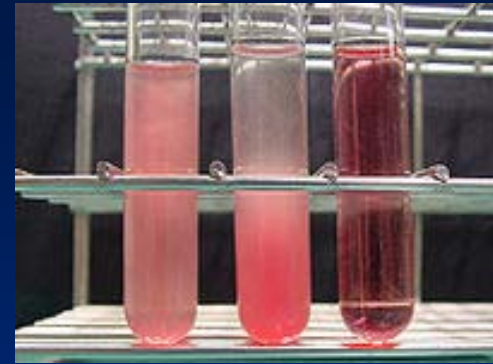
Hemolysis:

inherited vs acquired causes

→ premature/accelerated destruction of RBCs
(<100 d vs 110-120D)

- Hereditary hemolytic disorders:
 - RBC enzymes—G6PD
 - RBC membranes-spherocytosis
 - Hemoglobinopathies—SCC

Hemolysis



➤ Acquired Hemolytic disorders:

- Autoimmune hemolytic Anemia
- Microangiopathic hemolytic anemia
- Direct toxic effect---Malaria, clostridial etc

Autoimmune Hemolytic Anemia

Diagnosis:

- Hemolysis: LDH, lo hapto—90% specific for hemolysis
- NI LDH, hapto—92% sensitive for lack of hemolysis
- bil, reticulocyte, anemia
- +Coombs test—only test definitive of immune hemolysis



AIHA

Autoantibodies—2 major types:

- IgG--bind protein ag, body temperature, warm agglutinins
- IgM--bind polysaccharide ag, below body core temperature, cold agglutinins



Autoimmune Hemolytic Anemia

➤ Cold-reactive :

- IgM complement-fixing Ab
- Most common cold agglutinins are anti-I
- Ab+RBCs → agglutination at low tem.(4c)
- Warming leads to quick disagglutination
- eg: mycoplasma pneumonia, lymphoma

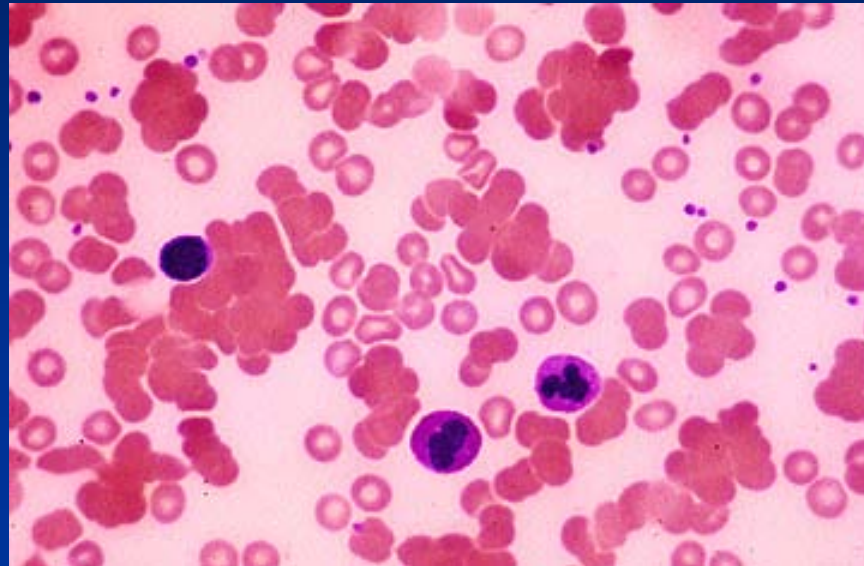


Normal Smear



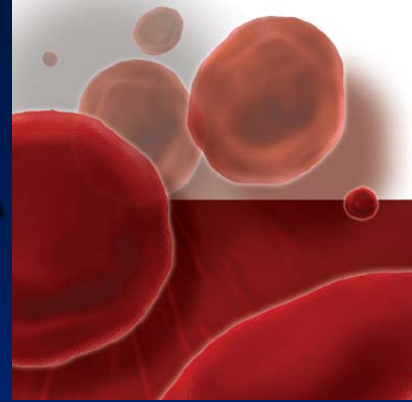
Normal peripheral blood smear.

Cold Agglutinin



Peripheral blood smear from a patient with cold agglutinin hemolytic anemia shows marked RBC agglutination into irregular clumps.

Warm antibody AIHA

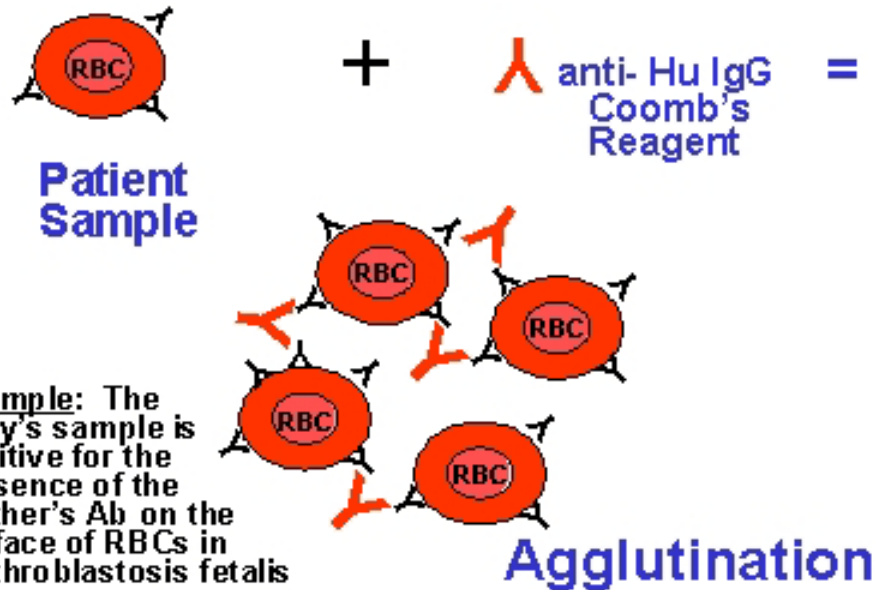


- IgG Abs against RBCs at body temp./37C
- Ab-coated RBCs removed by macrophages in the spleen
- RBC membrane change on binding to macrophages-→ spherocytes



DAT

DIRECT COOMB'S TEST



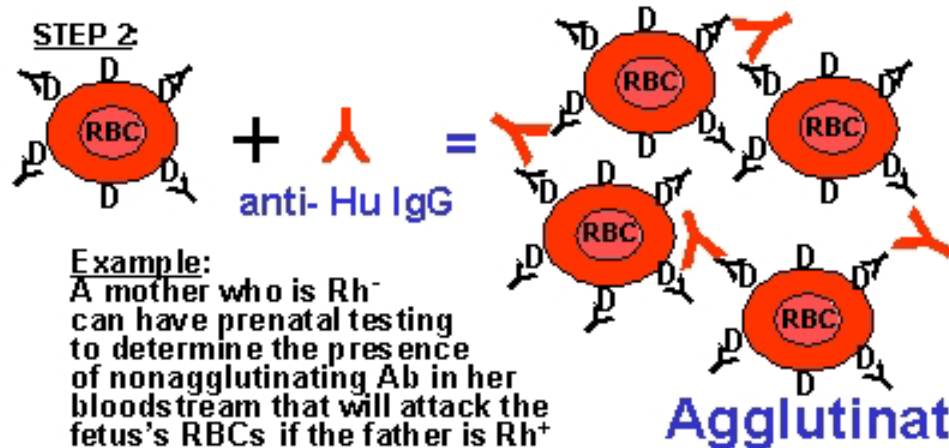
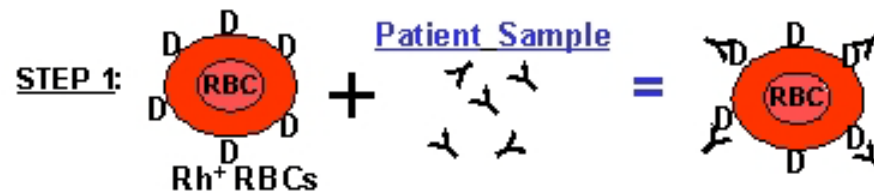
- Sensitivity/Specificity:

>99% patients with warm agglutinin AIHA will exhibit a positive result;

<1% normal population have + result.

Indirect Coomb's Test

INDIRECT COOMB'S TEST



Example:

A mother who is Rh⁻ can have prenatal testing to determine the presence of nonagglutinating Ab in her bloodstream that will attack the fetus's RBCs if the father is Rh⁺

Warm antibody AIHA

Etiology:

- Idiopathic--mostly
- Viral infections (usually in children)
- connective tissue ds. (esp SLE)
- Lymphoproliferative ds. (CLL etc)
- blood transfusion or Allo. SCT
- drugs



Etiology: drugs

Antibiotics:

- *PCN*
- *Ampicillin, amoxicillin*
- *cefazolin, cefotetan*
- *Sulfonamides*
- *Tetracycline*



Etiology: drugs

Chemo/biological agents

- *Fluorouracil*
- *Cisplatin/Carboplatin*
- *Cladribine*
- *oxaliplatin*
- *Interferon*
- *IL-2*



Etiology: drugs

Others:

- *Tylenol,*
- *Ibuprofen*
- *Insulin*
- *Levodopa*
- *etc*



Treatment



Treatment

- Blood transfusion
- Reduction in antibody production
steroids, cytotoxic drugs, rituxan
- Reduction in antibody effectiveness
splenectomy, IVIG



Treatment

1. Steroids

- Initial treatment
- Induce remission 60-70%
- Dose: 1mg/kg/day pred or equivalent
- Onset: 1-3 wks w Hgb rising
- Taper: slowly over months-->10mg/day qod

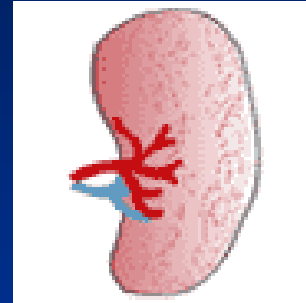


Treatment

2. Splenectomy

Effective in 60-70%

Usually within 2 weeks



3a. Cytotoxic agent

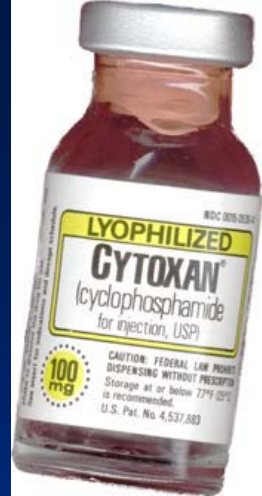
Cytosan:

1 month to be effective

Treatment

Cytoxan

- Nine patients failed a median of 3 other treatments.
- Cytoxan: 50 mg/kg/d x4 d
- median hemoglobin prior: 6.7 g/dL
- Six patients achieved complete remission and none have relapsed after a median follow-up of 15 months
- Three patients achieved and continue in partial remission (hemoglobin at least 10 g/dL without transfusion support).
- High-dose cyclophosphamide was well tolerated and induced durable remissions in patients with severe refractory autoimmune hemolytic anemia.



High-dose cyclophosphamide for refractory autoimmune hemolytic anemia.

Moyo VM et al. Blood 2002

Treatment



3b Rituxan:

14 patients w CLL-associated AIHA

rituximab: 375 mg/m²/wkly x 4

12 pts: increase in hgb levels 2nd to rituximab
(M:3.6 g/dl)

Onset: 2-4 weeks

Effective and well-tolerated

Rituximab therapy for CLL-associated autoimmune hemolytic anemia.

Am J Hematol. 2006 Jul

